August 14, 1956

Dear Bernie:

Thank you for sending me Gordon Allen's ms.

Frankly, I can see no reason why it should not be publishable, though I don't doubt you could suggest some minor polishings that might improve the ms. On the other hand, I can see why the editors might refuse to be enthusiastic about a purely speculative article, though, Goodness knows there have been enough of this genre on biopoiesis. I would agree that some authors have overstressed a "macromutational model" for the first step, but the conception of inorganic chemical evolution is by no means unique. In the last issue of the American Scientist, for example, Calvin has gone along this route, and I think you will find very similar ideas in my own review on Cell Heredity (Physiological Reviews, 32, at 424-426), which are expanded slightly in a discussion of "self-reproduction" in a soon-to-be-published Growth Society Symposium.

My own feelings about this topic are that it is time to stop talking and to start doing some experiments. Speculative ideas in this field are fairly prolific; one could probably found a journal that had nothing but. I can see why Am. Sc. might go against its better judgment to publish a such from Calvin, for he does at least speak from a background of substantial experimental work on relevant topics. In any case, American Naturalist is a poor journal to test the attitude of the scientific community; by its very nature it must reflect thepersonal tastes (and current space vacancies) as seen by the editors. It is easy to be discouraged or offended by having a paper rejected, but I know how easy it is to make mistakes (having sat on both sides of the fence). If Gordon is really deeply concerned about having this thing in print, he might just send it to a couple of other vehicles, e.g., Evolution, or if it were abbreviated somewhat, PNAS, and perhaps as a last resort Acta Biotheoretica (C.J. van der Klaauw, Zool. Lab., Kaiserstaat 63, Leiden, Holland) which sent me a very cordial letter a while ago inviting a contribution of just this sort. I am sure you could suggest others. For my own taste, while I have been willing to append thoughts like this to more deliberate reviews, I would hesitate about committing my energy and reputation to too elaborate an exposition without some experimental justification.

My own thinking about this problem has progressed slightly since 1952. It is almost too easy to find simple examples of self-dependence (reflexive catalysis); by themselves they make trivial models of evolution. We have to devise models whereby non-reflexive units can be compounded so as to make a more elaborate code, whose complexity can increase in evolution. I have thought that siloxane (S:O)= might be a more appropriate starting point than organic residues, simply because of its abundance and the ease with which diverse polysilicates are formed. There has been very little work on the conditions of growth of different kinds of silicate crystal, and I don't know whether this would fit the needs for the backbone structure; the problem has been to devise a mechanism by which a complex A-B-C-D augments the polymerization of such a complex, rather than just the A.B,C.D components. In a word (von Neumann's) we have to find a self-dependent "screw" which holds the

parts together. This is a somewhat different type of model from the others, but it is a direct reflection of the concept that genetic coding depends on the seriation of simple elements (in contemporary organisms, deoxynucleotides), that is on polymers, on compound rather than complex organic molecules. I agree that it seems unlikely that polynucleotides, as such, started life de novo, though the simplicity of recent work (ie Kornberg's) makes this more plausible than I would have thought two years ago.

This work on DNA synthesis suggests that a new start ought to be made on artificial biopoiesis, with more restricted goals still: namely to look for artificial systems which will directly imitate the proposals for polynucleotides. Are there simpler units, whose presence in the primeval ocean in activated form is more readily imaginable? If you could design a binary polymer where ABBA would augment the formation of this compound in a soup of A' + B', you would have a system that must evolve. Only then do you begin to worry how the supply of monomers is catalysed by the polymer, but as Archimedes didn't say, give me enough bits and I will give you "Methods of Enzymology".

This monologue is obviously addressed to Gordon, rather than yourself, but I thought you might care to add your own comments. Best wishes to both of you.

Yours sincerely,

Joshua Lederberg

P.S. I am enclosing the last page of the Amherst article, which should be in print some year now. Enough of that; on with the experiments!